VERSION WITH MARKINGS TO SHOW CHANGES MADE

(<u>Added material</u> is noted in bold underline; [deleted material] is noted in brackets)

In the Specification:

Please replace the paragraph beginning on page 4, line 17, with the following rewritten paragraph:

--OPGL is synthesised as a type II transmembrane protein consisting of 317 amino acid residues (human, cf. SEQ ID NO: 2 (corresponding DNA sequence in SEQ ID NO: 1) or 316 amino acid residues (murine, cf. SEQ ID NOs: 4 and 6 (corresponding DNA sequences in SEQ ID NOS: 3 and 5, respectively). Alignment of the two amino acid sequences show that identical amino acid residues are found at 87% of the homologous positions.--

Please replace the paragraph beginning on page 24, line 20, with the following rewritten paragraph:

--The promiscuous epitope can according to the invention be a naturally occurring human T-cell epitope such as epitopes from tetanus toxoid (e.g. the P2 and P30 epitopes (SEQ ID NOS: 34 and 35, respectively), diphtheria toxoid, Influenza virus hemagluttinin (HA), and P. falciparum CS antigen. --

Please replace the paragraph beginning on page 25, line 31, with the following rewritten paragraph:

--One especially preferred PADRE peptide is the one having the amino acid sequence AKFVAAWTLKAAA (SEQ ID NO: 36) or an immunologically effective subsequence thereof. This, and other epitopes having the same lack of MHC restriction are preferred T-cell epitopes which should be present in the OPGL analogues used in the inventive method. Such super-promiscuous epitopes will allow for the most simple embodiments of the invention wherein only one single modified OPGL is presented to the vaccinated animal's immune system.--

Please replace the paragraph beginning on page 54, line 18, with the following rewritten paragraph:

--A synthetic cDNA encoding the murine OPGL residues 158-316 has been synthesized removing sub-optimal *Eschericia coli* and *Pichia pastoris* codons from the published sequence. Additionally, an N-terminal Histidine tag, part of the cleavage site of the alpha mating factor signal sequence from *Sacharomyces cerevisiae*, and suitable restriction enzymes have been incorporated into the open reading frame (cf. SEQ ID NO: 7 (corresponding amino acid sequence in SEQ ID NO: 8)).--

Please replace the paragraph beginning on page 54, line 25, with the following rewritten paragraph:

--This cDNA encoding wild type murine OPGL has been cloned into a standard Eschericia coli expression vector (pTrc99a) using BspHI and HindIII restriction enzymes and a standard cloning vector (pBluescript KS+) using SacI and KpnI restriction enzymes (yielding SEQ ID NO: 9 (corresponding amino acid sequence in SEQ ID NO: 10)).--

Please replace the paragraph beginning on page 58, line 5, with the following rewritten paragraph:

--PCR of SEQ ID NO: 9 was performed using SEQ ID NOs: 22 and 25 as primers. The resulting PCR fragment was restriction digested with SacII and KpnI and subsequently purified from an agarose gel. A second PCR using SEQ ID NO: 9 as template was performed using primer SEQ ID NO: 26 and a vector specific primer. The resulting PCR fragment was restriction digested with KpnI and HindIII. Both fragments were then ligated to SEQ ID NO: 9 in pBluescript KS+ restriction digested with SacII and HindIII. To correct a single base mutation in this construct, PCR using the construct as template was performed with primers SEQ ID NOs: 33 and 29. The resulting PCR fragment was restriction digested with PstI + EcoRI, gel purified and subsequently ligated to the erroneous construct digested with PstI and EcoRI. The verified construct (SEQ ID NO: 13 (corresponding amino acid sequence in SEQ ID NO: 14) was then transferred to pTrc99a using BspHI and HindIII restriction enzymes.--

Please replace the paragraph beginning on page 58, line 23, with the following rewritten paragraph:

--PCR was performed using primers SEQ ID NOs: 27 and 28 without template. The resulting PCR fragment was restriction digested with *Pst*I and *Eco*RI and subsequently purified from an agarose gel. The resulting fragment was then ligated to SEQ ID NO: 9 in pBluescript KS+ restriction digested with

SacII and HindIII. The verified construct (SEQ ID NO: 15 (corresponding amino acid sequence in SEQ ID NO: 16) was subsequently transferred to pTrc99a using BspHI and HindIII restriction enzymes.--

Please replace the paragraph beginning on page 59, line 1, with the following rewritten paragraph:

--PCR of SEQ ID NO: 9 was performed using primers SEQ ID NOs: 22 and 29. The resulting PCR fragment was restriction digested with PstI and BstBI and subsequently purified from an agarose gel. A second PCR using SEQ ID NO: 9 as template was performed using primer SEQ ID NO: 30 and a vector specific primer. The resulting PCR fragment was restriction digested with BstBI and KpnI and subsequently gel purified. Both fragments were then ligated to SEQ ID NO: 9 in pBluescript KS+ restriction digested with PstI and KpnI. The verified construct (SEQ ID NO: 17 (corresponding amino acid sequence in SEQ ID NO: 18)) was then transferred to pTrc99a using BspHI and HindIII restriction enzymes.--

Please replace the paragraph beginning on page 59, line 14, with the following rewritten paragraph:

--PCR of SEQ ID NO: 9 was performed using primers SEQ ID NOs: 22 and 23. The resulting PCR fragment was restriction digested with SacII and KpnI and subsequently purified from an agarose gel. A second PCR using SEQ ID NO: 9 as template was performed using primer SEQ ID NOs: 24 and 31. The PCR fragment was restriction digested with KpnI and EcoRI and subsequently gel purified. Both fragments were then ligated to SEQ ID NO: 9 in

pBluescript KS+ restriction digested with SacII and EcoRI. The verified construct (SEQ ID NO: 19 (corresponding amino acid sequence in SEQ ID NO: 20) was then transferred to pTrc99a using BspHI and HindIII restriction enzymes.—

In the Claims:

Please replace Claim 12 with the following amended claim:

Claim 12 (amended) -- The method according to claim 11, wherein the natural T-cell epitope is selected from a Tetanus toxoid epitope such as P2 or P30 (SEQ ID NOS: 34 and 35, respectively), a diphtheria toxoid epitope, an influenza virus hemagluttinin epitope, and a P. falciparum CS epitope. --



SEQUENCE LISTING

M&E Biotech A/S HALKIER, Torben HAANING, Jesper

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<140> US 09/787,126

<141> 2001-03-14

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Asp Ser Cys Arg Arg Met Lys Gln Ala Phe Gln Gly Ala Val Gln Lys
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Glu Leu Gln His Ile Val Gly Pro Gln Arg Phe Ser Gly Ala Pro Ala
                       135
                                           140
Met Met Glu Gly Ser Trp Leu Asp Val Ala Gln Arg Gly Lys Pro Glu
                    150
                                        155
Ala Gln Pro Phe Ala His Leu Thr Ile Asn Ala Ala Ser Ile Pro Ser
                                    170
Gly Ser His Lys Val Thr Leu Ser Ser Trp Tyr His Asp Arg Gly Trp
           180
                               185
Ala Lys Ile Ser Asn Met Thr Leu Ser Asn Gly Lys Leu Arg Val Asn
                           200
Gln Asp Gly Phe Tyr Tyr Leu Tyr Ala Asn Ile Cys Phe Arg His His
                        215
                                            220
Glu Thr Ser Gly Ser Val Pro Thr Asp Tyr Leu Gln Leu Met Val Tyr
                    230
                                        235
Val Val Lys Thr Ser Ile Lys Ile Pro Ser Ser His Asn Leu Met Lys
                245
                                    250
Gly Gly Ser Thr Lys Asn Trp Ser Gly Asn Ser Glu Phe His Phe Tyr
                               265
Ser Ile Asn Val Gly Gly Phe Phe Lys Leu Arg Ala Gly Glu Glu Ile
                            280
                                               285
Ser Ile Gln Val Ser Asn Pro Ser Leu Leu Asp Pro Asp Gln Asp Ala
                       295
                                            300
Thr Tyr Phe Gly Ala Phe Lys Val Gln Asp Ile Asp
                    310
<210> 7
<211> 564
<212> DNA
<213> Artificial Sequence
<220>
<221> CDS
<222> (1)..(564)
<220>
<223> Description of Artificial Sequence: Synthetic PCR
     product with optimum codons for E. coli and P.
     pastoris expression
<220>
<221> misc binding
<222> (43)..(84)
<223> His tag
<220>
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<221> misc feature
<222> (1)..(36)
<223> C-terminal part of Saccharomyces cerevisiae
      alpha-mating factor
<220>
<221> misc feature
<222> (85)..(561)
<223> Encoding wild type murine OPGL, residues 158-316
<400> 7
gag etc gga tec etc gag aaa aga gag get gaa get eat gte atg aaa
                                                                   48
Glu Leu Gly Ser Leu Glu Lys Arg Glu Ala Glu Ala His Val Met Lys
                                     10
                                                                   96
cac caa cac caa cat caa cat caa cat caa cat caa aaa cct gaa gct
His Gln His Gln His Gln His Gln His Gln Lys Pro Glu Ala
                                 25
cag cca ttc gct cat ctg acc atc aac gct gca tcg atc cct tct ggt
                                                                   144
Gln Pro Phe Ala His Leu Thr Ile Asn Ala Ala Ser Ile Pro Ser Gly
tot cat aaa gtt acc ctg tot tot tgg tat cac gac cgc ggt tgg gct
                                                                   192
Ser His Lys Val Thr Leu Ser Ser Trp Tyr His Asp Arg Gly Trp Ala
     50
                         55
aaa atc tct aac atg acc ctg tct aac ggt aaa ctg aga gtt aac cag
                                                                   240
Lys Ile Ser Asn Met Thr Leu Ser Asn Gly Lys Leu Arg Val Asn Gln
                     70
                                          75
gac ggt ttc tac tac ctg tac gct aac atc tgt ttc aga cat cac gaa
                                                                   288
Asp Gly Phe Tyr Tyr Leu Tyr Ala Asn Ile Cys Phe Arg His His Glu
                 85
                                     90
ace tet ggt tet gtt eea ace gae tae etg eag etg atg gtt tae gtt
                                                                   336
Thr Ser Gly Ser Val Pro Thr Asp Tyr Leu Gln Leu Met Val Tyr Val
            100
                                105
gtt aaa acc tct atc aaa atc cca tct tca cat aac ctg atg aaa ggt
                                                                   384
Val Lys Thr Ser Ile Lys Ile Pro Ser Ser His Asn Leu Met Lys Gly
                            120
ggt tot acc aaa aac tgg tot ggt aac tot gaa tto cat tto tac tot
Gly Ser Thr Lys Asn Trp Ser Gly Asn Ser Glu Phe His Phe Tyr Ser
    130
                        135
                                             140
atc aac gtt ggt ggt ttc ttc aaa ctg aga gct ggt gaa gaa atc tct
                                                                   480
Ile Asn Val Gly Gly Phe Phe Lys Leu Arg Ala Gly Glu Glu Ile Ser
                    150
                                         155
ate cag gtt tet aac eet tet etg etg gae eea gae eag gae get ace
                                                                   528
Ile Gln Val Ser Asn Pro Ser Leu Leu Asp Pro Asp Gln Asp Ala Thr
                165
                                    170
tac ttc ggg gcc ttc aaa gtt cag gac atc gac tag
                                                                   564
Tyr Phe Gly Ala Phe Lys Val Gln Asp Ile Asp
<210> 8
<211> 187
<212> PRT
<213> Artificial Sequence
<220>
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<223> Description of Artificial Sequence: Synthetic PCR
product with optimum codons for E. coli and P.

pastoris expression

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<400> 8
Glu Leu Gly Ser Leu Glu Lys Arg Glu Ala Glu Ala His Val Met Lys
                                     10
His Gln His Gln His Gln His Gln His Gln Lys Pro Glu Ala
             20
                                 25
                                                     30
Gln Pro Phe Ala His Leu Thr Ile Asn Ala Ala Ser Ile Pro Ser Gly
                             40
Ser His Lys Val Thr Leu Ser Ser Trp Tyr His Asp Arg Gly Trp Ala
                         55
Lys Ile Ser Asn Met Thr Leu Ser Asn Gly Lys Leu Arg Val Asn Gln
                    70
Asp Gly Phe Tyr Tyr Leu Tyr Ala Asn Ile Cys Phe Arg His His Glu
                85
                                     90
Thr Ser Gly Ser Val Pro Thr Asp Tyr Leu Gln Leu Met Val Tyr Val
                                                    110
           100
                                105
Val Lys Thr Ser Ile Lys Ile Pro Ser Ser His Asn Leu Met Lys Gly
                           120
Gly Ser Thr Lys Asn Trp Ser Gly Asn Ser Glu Phe His Phe Tyr Ser
                        135
                                            140
Ile Asn Val Gly Gly Phe Phe Lys Leu Arg Ala Gly Glu Glu Ile Ser
                    150
                                        155
Ile Gln Val Ser Asn Pro Ser Leu Leu Asp Pro Asp Gln Asp Ala Thr
                                    170
                165
Tyr Phe Gly Ala Phe Lys Val Gln Asp Ile Asp
<210> 9
<211> 519
<212> DNA
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: DNA encoding
     murine OPGL, residues 158-316, fused to His tag
<220>
<221> CDS
<222> (1)..(519)
<220>
<221> misc binding
<222> (1)..(42)
<223> His tag
<220>
<221> misc feature
<222> (43)..(519)
<223> Murine OPGL, residues 158-316
<400> 9
atg aaa cac caa cac caa cat caa cat caa cat caa cat caa aaa cct
Met Lys His Gln His Gln His Gln His Gln His Gln His Gln Lys Pro
                                     10
gaa get cag eca tte get cat etg ace ate aac get gea teg ate eet
                                                                   96
```

```
Glu Ala Gln Pro Phe Ala His Leu Thr Ile Asn Ala Ala Ser Ile Pro
                                  25
                                                                    144
tct ggt tct cat aaa gtt acc ctg tct tct tgg tat cac gac cgc ggt
Ser Gly Ser His Lys Val Thr Leu Ser Ser Trp Tyr His Asp Arg Gly
                              40
tgg gct aaa atc tct aac atg acc ctg tct aac ggt aaa ctg aga gtt
Trp Ala Lys Ile Ser Asn Met Thr Leu Ser Asn Gly Lys Leu Arg Val
     50
                          55
                                                                    240
aac cag gac ggt ttc tac tac ctg tac gct aac atc tgt ttc aga cat
Asn Gln Asp Gly Phe Tyr Tyr Leu Tyr Ala Asn Ile Cys Phe Arg His
                     70
                                          75
cac gaa acc tot ggt tot gtt cca acc gac tac ctg cag ctg atg gtt
                                                                    288
His Glu Thr Ser Gly Ser Val Pro Thr Asp Tyr Leu Gln Leu Met Val
                 85
                                      90
tac gtt gtt aaa acc tct atc aaa atc cca tct tca cat aac ctg atg
                                                                    336
Tyr Val Val Lys Thr Ser Ile Lys Ile Pro Ser Ser His Asn Leu Met
            100
                                 105
aaa ggt ggt tct acc aaa aac tgg tct ggt aac tct gaa ttc cat ttc
                                                                    384
Lys Gly Gly Ser Thr Lys Asn Trp Ser Gly Asn Ser Glu Phe His Phe
                             120
tac tct atc aac gtt ggt ggt ttc ttc aaa ctg aga gct ggt gaa gaa
                                                                    432
Tyr Ser Ile Asn Val Gly Gly Phe Phe Lys Leu Arg Ala Gly Glu Glu
    130
                         135
atc tct atc cag gtt tct aac cct tct ctg ctg gac cca gac cag gac
                                                                    480
Ile Ser Ile Gln Val Ser Asn Pro Ser Leu Leu Asp Pro Asp Gln Asp
                    150
                                         155
gct acc tac ttc ggg gcc ttc aaa gtt cag gac atc gac
                                                                    519
Ala Thr Tyr Phe Gly Ala Phe Lys Val Gln Asp Ile Asp
                165
                                     170
<210> 10
<211> 173
<212> PRT
<213> Artificial Sequence
<223> Description of Artificial Sequence: DNA encoding
     murine OPGL, residues 158-316, fused to His tag
<400> 10
Met Lys His Gln His Gln His Gln His Gln His Gln His Gln Lys Pro
Glu Ala Gln Pro Phe Ala His Leu Thr Ile Asn Ala Ala Ser Ile Pro
                                  25
             20
Ser Gly Ser His Lys Val Thr Leu Ser Ser Trp Tyr His Asp Arg Gly
                              40
Trp Ala Lys Ile Ser Asn Met Thr Leu Ser Asn Gly Lys Leu Arg Val
                          55
Asn Gln Asp Gly Phe Tyr Tyr Leu Tyr Ala Asn Ile Cys Phe Arg His
                      70
                                          75
His Glu Thr Ser Gly Ser Val Pro Thr Asp Tyr Leu Gln Leu Met Val
                                      90
Tyr Val Val Lys Thr Ser Ile Lys Ile Pro Ser Ser His Asn Leu Met
                                 105
                                                     110
            100
Lys Gly Gly Ser Thr Lys Asn Trp Ser Gly Asn Ser Glu Phe His Phe
```

```
Tyr Ser Ile Asn Val Gly Gly Phe Phe Lys Leu Arg Ala Gly Glu Glu
                        135
Ile Ser Ile Gln Val Ser Asn Pro Ser Leu Leu Asp Pro Asp Gln Asp
                   150
                                        155
Ala Thr Tyr Phe Gly Ala Phe Lys Val Gln Asp Ile Asp
<210> 11
<211> 519
<212> DNA
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: Fusion of
      murine OPGL, residues 158-316 with C to S
      mutation, and His tag
<220>
<221> CDS
<222> (1)..(519)
<220>
<221> misc binding
<222> (1)..(42)
<223> His tag
<220>
<221> misc feature
<222> (43)..(228)
<223> Murine OPGL, residues 158-219
<220>
<221> misc feature
<222> (232)..(519)
<223> Murine OPGL, residues 221-316
<220>
<221> mutation
<222> (229)..(231)
<223> tgt (Cys) to tcc (Ser)
<220>
atg aaa cac caa cac caa cat caa cat caa cat caa cat caa aaa cct
                                                                   48
Met Lys His Gln His Gln His Gln His Gln His Gln His Gln Lys Pro
                                     10
gaa get cag cca tte get cat etg ace ate aac get gea teg ate eet
                                                                   96
Glu Ala Gln Pro Phe Ala His Leu Thr Ile Asn Ala Ala Ser Ile Pro
tot ggt tot cat aaa gtt acc ctg tot tot tgg tat cac gac cgc ggt
                                                                   144
Ser Gly Ser His Lys Val Thr Leu Ser Ser Trp Tyr His Asp. Arg Gly
                             40
tgg gct aaa atc tct aac atg acc ctg tct aac ggt aaa ctg aga gtt
                                                                   192
Trp Ala Lys Ile Ser Asn Met Thr Leu Ser Asn Gly Lys Leu Arg Val
```

aac cag gac ggt ttc tac tac ctg tac gct aac atc tcc ttc aga cat Asn Gln Asp Gly Phe Tyr Tyr Leu Tyr Ala Asn Ile Ser Phe Arg His 70 75 cac gaa acc tct ggt tct gtt cca acc gac tac ctg cag ctg atg gtt 288 His Glu Thr Ser Gly Ser Val Pro Thr Asp Tyr Leu Gln Leu Met Val 90 85 tac gtt gtt aaa acc tct atc aaa atc cca tct tca cat aac ctg atg 336 Tyr Val Val Lys Thr Ser Ile Lys Ile Pro Ser Ser His Asn Leu Met 100 105 aaa qqt qqt tct acc aaa aac tqq tct qqt aac tct qaa ttc cat ttc 384 Lys Gly Gly Ser Thr Lys Asn Trp Ser Gly Asn Ser Glu Phe His Phe 115 120 125 tac tct atc aac gtt ggt ggt ttc ttc aaa ctg aga gct ggt gaa gaa 432 Tyr Ser Ile Asn Val Gly Gly Phe Phe Lys Leu Arg Ala Gly Glu Glu 135 atc tct atc cag gtt tct aac cct tct ctg ctg gac cca gac cag gac 480 Ile Ser Ile Gln Val Ser Asn Pro Ser Leu Leu Asp Pro Asp Gln Asp 150 155 gct acc tac ttc ggg gcc ttc aaa gtt cag gac atc gac 519 Ala Thr Tyr Phe Gly Ala Phe Lys Val Gln Asp Ile Asp 165 <210> 12 <211> 173 <212> PRT <213> Artificial Sequence <220> <223> Description of Artificial Sequence: Fusion of murine OPGL, residues 158-316 with C to S mutation, and His tag <400> 12 Met Lys His Gln His Gln His Gln His Gln His Gln His Gln Lys Pro 10 Glu Ala Gln Pro Phe Ala His Leu Thr Ile Asn Ala Ala Ser Ile Pro 20 25 Ser Gly Ser His Lys Val Thr Leu Ser Ser Trp Tyr His Asp Arg Gly 40 Trp Ala Lys Ile Ser Asn Met Thr Leu Ser Asn Gly Lys Leu Arg Val 55 60 Asn Gln Asp Gly Phe Tyr Tyr Leu Tyr Ala Asn Ile Ser Phe Arg His His Glu Thr Ser Gly Ser Val Pro Thr Asp Tyr Leu Gln Leu Met Val 90 Tyr Val Val Lys Thr Ser Ile Lys Ile Pro Ser Ser His Asn Leu Met 100 105 110 Lys Gly Gly Ser Thr Lys Asn Trp Ser Gly Asn Ser Glu Phe His Phe 120 Tyr Ser Ile Asn Val Gly Gly Phe Phe Lys Leu Arg Ala Gly Glu Glu 140 135 Ile Ser Ile Gln Val Ser Asn Pro Ser Leu Leu Asp Pro Asp Gln Asp 150 155 Ala Thr Tyr Phe Gly Ala Phe Lys Val Gln Asp Ile Asp

170

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<210> 13
<211> 564
<212> DNA
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: Fusion of
      murine OPGL, residues 158-316 modified by
      introduction of tetanus toxoid P30 epitope, and
     His tag
<220>
<221> CDS
<222> (1)..(564)
<220>
<221> misc binding
<222> (1)..(42)
<223> His tag
<220>
<221> misc feature
<222> (43)..(336)
<223> Murine OPGL, residues 158-255
<220>
<221> misc feature
<222> (337)..(399)
<223> Tetanus toxoid P30 epitope
<220>
<221> misc_feature
<222> (400)..(564)
<223> Murine OPGL, residues 262-316
<400> 13
                                                                    48
atg aaa cac caa cac caa cat caa cat caa cat caa cat caa aaa cct
Met Lys His Gln His Gln His Gln His Gln His Gln His Gln Lys Pro
                  5
                                     10
gaa get cag eca tte get cat etg ace ate aac get gea teg ate eet
                                                                    96
Glu Ala Gln Pro Phe Ala His Leu Thr Ile Asn Ala Ala Ser Ile Pro
             20
                                 25
tot ggt tot cat aaa gtt acc ctg tot tot tgg tat cac gac cgc ggt
Ser Gly Ser His Lys Val Thr Leu Ser Ser Trp Tyr His Asp Arg Gly
                             40
tgg gct aaa atc tct aac atg acc ctg tct aac ggt aaa ctg aga gtt
                                                                    192
Trp Ala Lys Ile Ser Asn Met Thr Leu Ser Asn Gly Lys Leu Arg Val
     50
                         55
                                              60
aac cag gac ggt. ttc tac tac ctg tac gct aac atc tgt ttc aga cat
                                                                    240
Asn Gln Asp Gly Phe Tyr Tyr Leu Tyr Ala Asn Ile Cys Phe Arg His
cac gaa acc tot ggt tot gtt cca acc gac tac ctg cag ctg atg gtt
                                                                    288
His Glu Thr Ser Gly Ser Val Pro Thr Asp Tyr Leu Gln Leu Met Val
                 85
                                     90
tac gtt gtt aaa acc tct atc aaa atc cca tct tca cat aac ctg atg
                                                                    336
Tyr Val Val Lys Thr Ser Ile Lys Ile Pro Ser Ser His Asn Leu Met
```

```
100
                                105
                                                     110
tto aac aac tto acc gtt tot tto tgg ctg agg gta ccg aaa gtt tot
                                                                   384
Phe Asn Asn Phe Thr Val Ser Phe Trp Leu Arg Val Pro Lys Val Ser
                            120
                                                 125
        115
gct tct cac ctg gaa aac tgg tct ggt aac tct gaa ttc cat ttc tac
                                                                   432
Ala Ser His Leu Glu Asn Trp Ser Gly Asn Ser Glu Phe His Phe Tyr
                        135
tct atc aac gtt ggt ggt ttc ttc aaa ctg aga gct ggt gaa gaa atc
                                                                   480
Ser Ile Asn Val Gly Gly Phe Phe Lys Leu Arg Ala Gly Glu Glu Ile
145
                    150
                                        155
tot ato cag gtt tot aac cot tot otg otg gac coa gac cag gac got
                                                                   528
Ser Ile Gln Val Ser Asn Pro Ser Leu Leu Asp Pro Asp Gln Asp Ala
                                    170
                165
                                                                   564
acc tac ttc ggg gcc ttc aaa gtt cag gac atc gac
Thr Tyr Phe Gly Ala Phe Lys Val Gln Asp Ile Asp
            180
                                185
<210> 14
<211> 188
<212> PRT
<213> Artificial Sequence
<223> Description of Artificial Sequence: Fusion of
      murine OPGL, residues 158-316 modified by
      introduction of tetanus toxoid P30 epitope, and
      His tag
<400> 14
Met Lys His Gln His Gln His Gln His Gln His Gln His Gln Lys Pro
                                     10
Glu Ala Gln Pro Phe Ala His Leu Thr Ile Asn Ala Ala Ser Ile Pro
             20
                                 25
Ser Gly Ser His Lys Val Thr Leu Ser Ser Trp Tyr His Asp Arg Gly
Trp Ala Lys Ile Ser Asn Met Thr Leu Ser Asn Gly Lys Leu Arg Val
                                              60
Asn Gln Asp Gly Phe Tyr Tyr Leu Tyr Ala Asn Ile Cys Phe Arg His
His Glu Thr Ser Gly Ser Val Pro Thr Asp Tyr Leu Gln Leu Met Val
                                     90
                 85
Tyr Val Val Lys Thr Ser Ile Lys Ile Pro Ser Ser His Asn Leu Met
                                105
Phe Asn Asn Phe Thr Val Ser Phe Trp Leu Arg Val Pro Lys Val Ser
                            120
                                                 125
Ala Ser His Leu Glu Asn Trp Ser Gly Asn Ser Glu Phe His Phe Tyr
                        135
                                             140
Ser Ile Asn Val Gly Gly Phe Phe Lys Leu Arg Ala Gly Glu Glu Ile
                    150
                                        155
Ser Ile Gln Val Ser Asn Pro Ser Leu Leu Asp Pro Asp Gln Asp Ala
                                     170
Thr Tyr Phe Gly Ala Phe Lys Val Gln Asp Ile Asp
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<210> 15

180

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<211> 546
<212> DNA
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: Fusion
      between murine OPGL, residues 158-316 with tetanus
      toxoid P2 epitope introduced, and His tag
<220>
<221> CDS
<222> (1)..(546)
<220>
<221> misc_binding
<222> (1)..(42)
<223> His tag
<220>
<221> misc feature
<222> (43)..(336)
<223> Murine OPGL, residues 158-255
<220>
<221> misc_feature
<222> (382)..(546)
<223> Murine OPGL, residues 262-316
<220>
<221> misc feature
<222> (337)..(381)
<223> Tetanus toxoid P2 epitope
<400> 15
atg aaa cac caa cac caa cat caa cat caa cat caa cat caa aaa cct
                                                                   48
Met Lys His Gln His Gln His Gln His Gln His Gln His Gln Lys Pro
                                     10
gaa get cag eea tte get cat etg ace ate aac get gea teg ate eet
Glu Ala Gln Pro Phe Ala His Leu Thr Ile Asn Ala Ala Ser Ile Pro
                                 25
tet ggt tet cat aaa gtt ace etg tet tet tgg tat cae gae ege ggt
                                                                   144
Ser Gly Ser His Lys Val Thr Leu Ser Ser Trp Tyr His Asp Arg Gly
         35
                             40
                                                  45
tgg gct aaa atc tct aac atg acc ctg tct aac ggt aaa ctg aga gtt
                                                                   192
Trp Ala Lys Ile Ser Asn Met Thr Leu Ser Asn Gly Lys Leu Arg Val
                         55
                                              60
                                                                   240
aac caq qac qqt ttc tac tac ctq tac qct aac atc tgt ttc aga cat
Asn Gln Asp Gly Phe Tyr Tyr Leu Tyr Ala Asn Ile Cys Phe Arg His
                                          75
                                                                   288
cac gaa acc tot ggt tot gtt cca acc gac tac ctg cag ctg atg gtt
His Glu Thr Ser Gly Ser Val Pro Thr Asp Tyr Leu Gln Leu Met Val
tac gtt gtt aaa acc cct atc aaa atc caa tct tca cat aac ctg atg
                                                                   336
Tyr Val Val Lys Thr Pro Ile Lys Ile Gln Ser Ser His Asn Leu Met
            100
                                 105
cag tac atc aaa gct aat tcg aaa ttc atc ggt atc acc gaa ctg aac
                                                                   384
Gln Tyr Ile Lys Ala Asn Ser Lys Phe Ile Gly Ile Thr Glu Leu Asn
```

```
125
       115
                            120
tgg tot ggt aac tot gaa tto cat tto tac tot ato aac gtt ggt ggt
Trp Ser Gly Asn Ser Glu Phe His Phe Tyr Ser Ile Asn Val Gly Gly
                       135
                                            140
   130
ttc ttc aaa ctg aga gct ggt gaa gaa atc tct atc cag gtt tct aac
Phe Phe Lys Leu Arg Ala Gly Glu Glu Ile Ser Ile Gln Val Ser Asn
                    150
                                        155
cct tct ctg ctg gac cca gac cag gac gct acc tac ttc ggg gcc ttc
Pro Ser Leu Leu Asp Pro Asp Gln Asp Ala Thr Tyr Phe Gly Ala Phe
                165
                                    170
aaa gtt cag gac atc gac
Lys Val Gln Asp Ile Asp
            180
<210> 16
<211> 182
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: Fusion
      between murine OPGL, residues 158-316 with tetanus
      toxoid P2 epitope introduced, and His tag
<400> 16
Met Lys His Gln His Gln His Gln His Gln His Gln His Gln Lys Pro
                                     10
Glu Ala Gln Pro Phe Ala His Leu Thr Ile Asn Ala Ala Ser Ile Pro
            20
                                 25
Ser Gly Ser His Lys Val Thr Leu Ser Ser Trp Tyr His Asp Arg Gly
                             40
Trp Ala Lys Ile Ser Asn Met Thr Leu Ser Asn Gly Lys Leu Arg Val
                         55
                                             60
Asn Gln Asp Gly Phe Tyr Tyr Leu Tyr Ala Asn Ile Cys Phe Arg His
                     70
                                         75
His Glu Thr Ser Gly Ser Val Pro Thr Asp Tyr Leu Gln Leu Met Val
                                     90
                 85
Tyr Val Val Lys Thr Pro Ile Lys Ile Gln Ser Ser His Asn Leu Met
Gln Tyr Ile Lys Ala Asn Ser Lys Phe Ile Gly Ile Thr Glu Leu Asn
                            120
Trp Ser Gly Asn Ser Glu Phe His Phe Tyr Ser Ile Asn Val Gly Gly
                        135
                                            140
Phe Phe Lys Leu Arg Ala Gly Glu Glu Ile Ser Ile Gln Val Ser Asn
                    150
                                        155
Pro Ser Leu Leu Asp Pro Asp Gln Asp Ala Thr Tyr Phe Gly Ala Phe
                165
                                    170
Lys Val Gln Asp Ile Asp
            180
<210> 17
<211> 519
<212> DNA
```

480

528

546

<213> Artificial Sequence

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<220>
<223> Description of Artificial Sequence: Fusion between
     murine OPGL, residues 158-316 with tetanus toxoid
      P2 epitope introduced, and His tag
<220>
<221> CDS
<222> (1)..(519)
<220>
<221> misc binding
<222> (1)..(42)
<223> His tag
<220>
<221> misc feature
<222> (43)..(432)
<223> Murine OPGL, residues 158-287
<220>
<221> misc feature
<222> (478)..(519)
<223> Murine OPGL, residues 303-316
<220>
<221> misc feature
<222> (433)..(477)
<223> Tetanus toxoid P2 epitope
<400> 17
atg aaa cac caa cac caa cat caa cat caa cat caa cat caa aaa cct
                                                                    48
Met Lys His Gln His Gln His Gln His Gln His Gln His Gln Lys Pro
                                      10
                                                                    96
gaa get cag eca tte get cat etg ace ate aac get gea teg ate eet
Glu Ala Gln Pro Phe Ala His Leu Thr Ile Asn Ala Ala Ser Ile Pro
             20
tot ggt tot cat aaa gtt acc ctg tot tot tgg tat cac gac cgc ggt
                                                                    144
Ser Gly Ser His Lys Val Thr Leu Ser Ser Trp Tyr His Asp Arg Gly
tgg gct aaa atc tct aac atg acc ctg tct aac ggt aaa ctg aga gtt
                                                                    192
Trp Ala Lys Ile Ser Asn Met Thr Leu Ser Asn Gly Lys Leu Arg Val
     50
                         55
                                              60
aac cag gac ggt ttc tac tac ctg tac gct aac atc tgt ttc aga cat
                                                                    240
Asn Gln Asp Gly Phe Tyr Tyr Leu Tyr Ala Asn Ile Cys Phe Arg His
                     70
                                          75
cac gaa acc tet ggt tet gtt eca acc gae tae etg eag etg atg gtt
                                                                    288
His Glu Thr Ser Gly Ser Val Pro Thr Asp Tyr Leu Gln Leu Met Val
                                      90
                 8.5
tac gtt gtt aaa acc tct atc aaa atc cca tct tca cat aac ctg atg
                                                                    336
Tyr Val Val Lys Thr Ser Ile Lys Ile Pro Ser Ser His Asn Leu Met
            100
                                 105
                                                     110
aaa ggt ggt tct acc aaa aac tgg tct ggt aac tct gaa ttc cat ttc
                                                                    384
Lys Gly Gly Ser Thr Lys Asn Trp Ser Gly Asn Ser Glu Phe His Phe
                            120
                                                 125
        115
                                                                    432
tac tct atc aac gtt ggt ggt ttc ttc aaa ctg aga gct ggt gaa gaa
Tyr Ser Ile Asn Val Gly Gly Phe Phe Lys Leu Arg Ala Gly Glu Glu
                        135
                                             140
```

```
cag tac atc aaa gct aat tcg aaa ttc atc ggt atc acc gaa ctg gac
Gln Tyr Ile Lys Ala Asn Ser Lys Phe Ile Gly Ile Thr Glu Leu Asp
                    150
                                        155
                                                                   519
gct acc tac ttc ggg gcc ttc aaa gtt cag gac atc gac
Ala Thr Tyr Phe Gly Ala Phe Lys Val Gln Asp Ile Asp
<210> 18
<211> 173
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: Fusion between
      murine OPGL, residues 158-316 with tetanus toxoid
      P2 epitope introduced, and His tag
<400> 18
Met Lys His Gln His Gln His Gln His Gln His Gln His Gln Lys Pro
                                     10
                                                          15
Glu Ala Gln Pro Phe Ala His Leu Thr Ile Asn Ala Ala Ser Ile Pro
Ser Gly Ser His Lys Val Thr Leu Ser Ser Trp Tyr His Asp Arg Gly
                             40
Trp Ala Lys Ile Ser Asn Met Thr Leu Ser Asn Gly Lys Leu Arg Val
Asn Gln Asp Gly Phe Tyr Tyr Leu Tyr Ala Asn Ile Cys Phe Arg His
                     70
                                         75
His Glu Thr Ser Gly Ser Val Pro Thr Asp Tyr Leu Gln Leu Met Val
                                     90
Tyr Val Val Lys Thr Ser Ile Lys Ile Pro Ser Ser His Asn Leu Met
            100
                                105
                                                    110
Lys Gly Gly Ser Thr Lys Asn Trp Ser Gly Asn Ser Glu Phe His Phe
                            120
Tyr Ser Ile Asn Val Gly Gly Phe Phe Lys Leu Arg Ala Gly Glu Glu
                        135
                                            140
Gln Tyr Ile Lys Ala Asn Ser Lys Phe Ile Gly Ile Thr Glu Leu Asp
                    150
                                        155
Ala Thr Tyr Phe Gly Ala Phe Lys Val Gln Asp Ile Asp
                165
                                    170
<210> 19
<211> 519
<212> DNA
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: Fusion between
      murine OPGL, residues 158-316 with tetanus toxoid
      P30 epitope introduced, and His tag
<220>
<221> CDS
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<222> (1)..(519)

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<220>
<221> misc binding
<222> (1)..(42)
<223> His tag
<220>
<221> misc_feature
<222> (43)..(231)
<223> Murine OPGL, residues 158-220
<220>
<221> misc feature
<222> (295)..(519)
<223> Murine OPGL, residues 242-316
<220>
<221> misc feature
<222> (232)..(294)
<223> Tetanus toxoid P30 epitope
<400> 19
atg aaa cac caa cac caa cat caa cat.caa cat caa cat caa aaa cct
Met Lys His Gln His Gln His Gln His Gln His Gln His Gln Lys Pro
                                     10
                                                                    96
qua qct caq cca ttc qct cat ctg acc atc aac gct gca tcg atc cct
Glu Ala Gln Pro Phe Ala His Leu Thr Ile Asn Ala Ala Ser Ile Pro
                                 25
tot ggt tot cat aaa gtt acc otg tot tot tgg tat cac gac ogc ggt
                                                                   144
Ser Gly Ser His Lys Val Thr Leu Ser Ser Trp Tyr His Asp Arg Gly
                             40
                                                                    192
tgg gct aaa atc tct aac atg acc ctg tct aac ggt aaa ctg aga gtt
Trp Ala Lys Ile Ser Asn Met Thr Leu Ser Asn Gly Lys Leu Arg Val
                                              60
                         55
aac cag gac ggt ttc tac tac ctg tac gct aac atc tgt ttc aac aac
Asn Gln Asp Gly Phe Tyr Tyr Leu Tyr Ala Asn Ile Cys Phe Asn Asn
                                          75
                     70
 65
                                                                    288
ttc acc gtt tct ttc tgg ctg agg gta ccg aaa gtt tct gct tct cac
Phe Thr Val Ser Phe Trp Leu Arg Val Pro Lys Val Ser Ala Ser His
                                      90
                 85
                                                                    336
ctq qaa gtt aaa acc tct atc aaa atc cca tct tca cat aac ctg atg
Leu Glu Val Lys Thr Ser Ile Lys Ile Pro Ser Ser His Asn Leu Met
                                105
            100
aaa ggt ggt tct acc aaa aac tgg tct ggt aac tct gaa ttc cat ttc
Lys Gly Gly Ser Thr Lys Asn Trp Ser Gly Asn Ser Glu Phe His Phe
        115
                            120
                                                 125
                                                                    432
tac tet ate aac gtt ggt ggt tte tte aaa etg aga get ggt gaa gaa
Tyr Ser Ile Asn Val Gly Gly Phe Phe Lys Leu Arg Ala Gly Glu Glu
                        135
                                             140
atc tct atc cag gtt tct aac cct tct ctg ctg gac cca gac cag gac
Ile Ser Ile Gln Val Ser Asn Pro Ser Leu Leu Asp Pro Asp Gln Asp
                                                             160
                                         155
145
                    150
                                                                    519
gct acc tac ttc ggg gcc ttc aaa gtt cag gac atc gac
Ala Thr Tyr Phe Gly Ala Phe Lys Val Gln Asp Ile Asp
                                     170
                165
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<212> PRT
<213> Artificial Sequence
<223> Description of Artificial Sequence: Fusion between
     murine OPGL, residues 158-316 with tetanus toxoid
      P30 epitope introduced, and His tag
<400> 20
Met Lys His Gln His Gln His Gln His Gln His Gln His Gln Lys Pro
                 5
                                     10
Glu Ala Gln Pro Phe Ala His Leu Thr Ile Asn Ala Ala Ser Ile Pro
                                 25
Ser Gly Ser His Lys Val Thr Leu Ser Ser Trp Tyr His Asp Arg Gly
                             40
Trp Ala Lys Ile Ser Asn Met Thr Leu Ser Asn Gly Lys Leu Arg Val
                         55
Asn Gln Asp Gly Phe Tyr Tyr Leu Tyr Ala Asn Ile Cys Phe Asn Asn
                                         75
                     70
Phe Thr Val Ser Phe Trp Leu Arg Val Pro Lys Val Ser Ala Ser His
                                     90
Leu Glu Val Lys Thr Ser Ile Lys Ile Pro Ser Ser His Asn Leu Met
            100
                                105
                                                     110
Lys Gly Gly Ser Thr Lys Asn Trp Ser Gly Asn Ser Glu Phe His Phe
                           120
Tyr Ser Ile Asn Val Gly Gly Phe Phe Lys Leu Arg Ala Gly Glu Glu
                        135
                                            140
Ile Ser Ile Gln Val Ser Asn Pro Ser Leu Leu Asp Pro Asp Gln Asp
                   150
                                        155
Ala Thr Tyr Phe Gly Ala Phe Lys Val Gln Asp Ile Asp
                165
                                    170
<210> 21
<211> 68
<212> DNA
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: Synthetic PCR
     primer
<400> 21
agctgcaggt agtcggttgg aacagaacca gaggtttcgt gatgtctgaa acagatgtta 60
gcgtacag
<210> 22
<211> 24
<212> DNA
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: Synthetic PCR
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<211> 173

primer

ctcatctgac catcaacgct gcat	24
<210> 23 <211> 64 <212> DNA <213> Artificial Sequence	
<220> <223> Description of Artificial Sequence: Synthetic PCR primer	
<400> 23 tttcggtacc ctcagccaga aagaaacggt gaagttgttg aaacagatgt tagcgtacag gtag	60 64
<210> 24 <211> 61 <212> DNA <213> Artificial Sequence	
<220> <223> Description of Artificial Sequence: Synthetic PCR primer	
<400> 24 tgagggtacc gaaagtttct gcttctcacc tggaagttaa aacccctatc aaaatccaat c	60 61
<pre> <210> 25 <211> 63 <212> DNA <213> Artificial Sequence </pre>	
<220> <223> Description of Artificial Sequence: Synthetic PCR primer	
<400> 25 tttcggtacc ctcagccaga aagaaacggt gaagttgttg aacatcaggt tatgtgaaga ttg	60 63
<210> 26 <211> 62 <212> DNA <213> Artificial Sequence	
<220> <223> Description of Artificial Sequence: Synthetic PCR primer	
<400> 26 tgagggtacc gaaagtttet getteteace tggaaaactg gtetggtaac tetgaattee	60

at

<210><211><211><212><212>	79	
\ 2137	Artificial Sequence	
	Description of Artificial Sequence: Synthetic PCR primer	
	27 gcagc tgatggttta cgttgttaaa acccctatca aaatccaatc ttcacataac gcagt acatcaaag	60 79
<210><211><211><212><213>	83	
<220> <223>	Description of Artificial Sequence: Synthetic PCR primer	
	28 ctcag agttaccaga ccagttcagt tcggtgatac cgatgaattt cgaattagct gtact gcatcaggtt atg	60 83
<210><211><211><212><213>	49	
<220> <223>	Description of Artificial Sequence: Synthetic PCR primer	
<400> gaattt	29 ccgaa ttagctttga tgtactgttc ttcaccagct ctcagtttg	49
<210> <211> <212> <213>	53	
<220> <223>	Description of Artificial Sequence: Synthetic PCR primer	
<400>	30	53

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<210> 31
<211> 26
<212> DNA
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: Synthetic PCR
      primer
<400> 31
cttactagtc gatgtcctga actttg
                                                                    26
<210> 32
<211> 74
<212> DNA
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: Synthetic PCR
      primer
<400> 32
agtggaattc agagttacca gaccagtttt tggtagaacc acctttcatc aggttatgtg 60
aagatgggat tttg
<210> 33
<211> 65
<212> DNA
<213> Clostridium tetani
<400> 33
actacctgca gctgatggtt tacgttgtta aaacctctat caaaatccca tcttcacata 60
                                                                    65
<210> 34
<211> 15
<212> PRT
<213> Clostridium tetani
<400> 34
Gln Tyr Ile Lys Ala Asn Ser Lys Phe Ile Gly Ile Thr Glu Leu
                                      10
<210> 35
<211> 21
<212> PRT
<213> Clostridium tetani
<400> 35
Phe Asn Asn Phe Thr Val Ser Phe Trp Leu Arg Val Pro Lys Val Ser
                                      10
                  5
Ala Ser His Leu Glu
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